# SUMMARY OF PRODUCT CHARACTERISTICS

## 1. NAME OF THE VETERINARY MEDICINAL PRODUCT

**Tilmovet 40 g/kg**
**Premix** for medicated feeding stuff for pigs and rabbits

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance: 40 g tilmicosin per kg
Excipients:

For the full list of excipients: see section 6.1

## 3. PHARMACEUTICAL FORM

Premix for medicated feeding stuff

A yellowish tan to reddish tan free-flowing granular material.

## 4. CLINICAL PARTICULARS

### 4.1 Target species

Pigs (weaned piglets and fattening pigs) and rabbits

### 4.2 Indications for use (specifying the target species)

Pigs:

Prevention and treatment of respiratory disease caused by *Actinobacillus pleuropneumoniae, Mycoplasma hyopneumoniae, Pasteurella multocida* and other organisms sensitive to tilmicosin

Rabbits:

Prevention and treatment of respiratory disease caused by *Pasteurella multocida and Bordetella bronchiseptica,* susceptible to tilmicosin.

### 4.3 Contraindications

Horses or other *Equidae*, must not be allowed access to feeds containing tilmicosin. Horses fed with tilmicosin medicated feeds may present signs of toxicity with lethargy, anorexia, reduction of feed consumption, loose stools, colic, distension of the abdomen and death.

Do not use in case of hypersensitivity to tilmicosin or to any of the excipients.

Do not use in animals hypersensitive to tilmicosin and when there is resistance to

tilmicosin or cross resistance to other macrolides like tylosin, erythromycin or lincomycin.

## 4.4 Special warnings (for each target species)

With regard to the management of respiratory disease outbreaks, it should be noted that acutely ill animals are likely to be inappetant and therefore require parenteral treatment.

## 4.5 Special precautions for use

### Special precautions for use in animals

Inappropriate use of the product may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with tilmicosin related substances.

Due to the likely variability (time, geographical) in the occurrence of the resistance of bacteria for tilmicosin, bacteriological sampling and susceptibility testing are recommended.

Cross-resistance between tilmicosin and other macrolide antibiotic has been observed. Use of the product should be based on susceptibility testing and take into account official, national and regional antimicrobial policies. Inappropriate use of the product may increase the prevalence of bacteria resistant to tilmicosin and may decrease the effectiveness of treatment with tilmicosin related substances.

### Special precautions for the person administering the veterinary medicinal product to animals

The handling of the product in case of known hypersensitivity to macrolide antibiotics must be avoided.
May cause sensitisation by skin contact. May cause skin and eye irritation. Avoid direct skin contact. Wear overalls, safety glasses and impervious gloves when mixing and handling the product. Wash affected parts if skin contact occurs. If accidental eye contact occurs, immediately rinse thoroughly with water. In case of accidental ingestion, or if you develop symptoms following exposure such as skin rash, seek medical advice immediately and show the package leaflet or the label to the physician. Swelling of the face, lips or eyes or difficulty with breathing are more serious symptoms and require urgent medical attention.
If the operations involve the risk of exposure to dust, wear either a disposable filter and half mask respirator conforming to European Standard EN149 or a non-disposable respirator to European Standard EN140 fitted with a filter to EN143. This warning is particularly relevant to on-farm mixing, where the risk of exposure to dust is likely to be enhanced.

## 4.6 Adverse reactions (frequency and seriousness)

In very rare cases (less than 1 animal in 10,000 animals), feed intake may decrease (including feed refusal) in animals receiving medicated feed. This effect is transient.

## 4.7 Use during pregnancy, lactation or lay

Laboratory studies in rats have not produced any evidence of a teratogenic, foetotoxic/embryotoxic effect of tilmicosin, however, a maternotoxicity was observed at doses that were close to the therapeutic dosage. The product is safe in sows whatever the pregnancy stages.

The safety of the veterinary medicinal product has not been established in boars used for breeding purposes.

## 4.8 Interaction with other medicinal products and other forms of interaction

Do not use simultaneously with other macrolides and lincosamides.
Do not use simultaneously with bacteriostatic antimicrobial agents.
Tilmicosin may decrease the antibacterial activity of β-lactam antibiotics.

## 4.9 Amount(s) to be administered and administration route

The uptake of medicated feed depends on the clinical condition of the animals. In order to obtain a correct dosage the concentration of tilmicosin has to be adjusted accordingly.
Use the following formula:

$$\text{Kg product/tone feed} = \frac{\text{Dose rate (mg/kg bodyweight) x bodyweight (kg)}}{\text{Daily feed intake (kg) x premix strength (g/kg)}}$$

**Pigs**
Administer in the feed at a dose of 8 to 16 mg/kg body weight/day of tilmicosin (equivalent to 200 to 400 ppm in the feed) for a period of 15 to 21 days.

| Indication | Dose of tilmicosin | Duration of treatment | Inclusion rate in feed |
|---|---|---|---|
| Prevention and treatment of respiratory disease | 8-16 mg/kg bodyweight/day | 15 to 21 days | 5-10 kg product/tonne |

**Rabbits**
Administer in the feed at 12 mg/kg body weight/day of tilmicosin (equivalent to 200 ppm in the feed) for 7 days.

| Indication | Dose of tilmicosin | Duration of treatment | Inclusion rate in feed |
|---|---|---|---|
| Prevention and treatment of respiratory disease | 12 mg/kg bodyweight/day | 7 days | 5 kg product /tonne |

To ensure thorough dispersion of the product, it should first be mixed with a suitable quantity of feed before incorporation into the finished feed.
This product can be incorporated into pelleted feed, preconditioned for the minimum time-period at a temperature not exceeding 75°C

## 4.10 Overdose (symptoms, emergency procedures, antidotes), if necessary

No symptoms of overdose have been seen in pigs fed a ration containing levels of tilmicosin up to 80 mg/kg bodyweight (equivalent to 2000 ppm in the feed or ten times

the recommended dose) for 15 days.

### 4.11 Withdrawal period(s)

Pigs: meat and offal: 21 days
Rabbits: meat and offal: 4 days

## 5. PHARMACOLOGICAL PROPERTIES

Pharmacotherapeutic group: antibacterials for systemic use; macrolides, tilmicosin

ATC vet code: QJ01FA91

### 5.1 Pharmacodynamic properties

Tilmicosin is a mainly bactericidal semi-synthetic antibiotic of the macrolide group. It is believed to affect the bacterial protein synthesis *in vitro* and *in vivo*, without affecting the nucleic acid synthesis. It is mostly bacteriostatic. It has a bactericidal effect on *Pasteurella* spp.

Tilmicosin has a wide spectrum of activity against Gram-positive organisms is particularly active against *Pasteurella, Actinobacillus (Haemophilus)* and *Mycoplasma* organisms of bovine, porcine and avian origin. Tilmicosin has some activity against certain Gram-negative micro-organisms.

Cross resistance between tilmicosin and other macrolide antibiotics has been observed. Macrolides inhibit protein synthesis by reversibly binding to the 50S ribosomal subunit. Bacterial growth is inhibited by induction of the separation of peptidyl transfer RNA from the ribosome during the elongation phase.
Ribosomal methylase, encoded by the *erm* gene, can precipitate resistance to macrolides by alteration of the ribosomal binding site.
The gene that encodes for an efflux mechanism, *mef*, also brings about a moderate degree of resistance.
Resistance is also brought about by an efflux pump that actively rids the cells of the macrolide. This efflux pump is chromosomally mediated by genes referred to as *acrAB* genes. Resistance of Pseudomonas species and other Gram-negative bacteria, enterococci and staphylococci may be precipitated by chromosomally controlled alteration of permeability or uptake of the drug.

## 5.2 Pharmacokinetic properties

**Pigs:**
Absorption: When administered to pigs via the oral route at a dose of 400 mg tilmicosin/kg feed (equivalent to approximately 21.3 mg tilmicosin/kg bodyweight/day), tilmicosin moves rapidly out of the serum into areas of low pH. The highest concentration in the serum (0.23 ±0.08 µg/ml) was recorded on day 10 of medication, but concentrations above the limit of quantification (0.10 µg/ml) were not found in 3 out of 20 animals examined. Lung concentrations increased rapidly between days 2 and 4 but no significant changes were obtained following four days of dosing. The maximum concentration in lung tissue (2.59±1.01 µg/ml) was recorded on day 10 of medication.

When administered at a dose of 200 mg tilmicosin/kg feed (equivalent to approximately 11.0 mg/kg/day), plasma concentrations above the limit of quantification (0.10 µg/ml) were found in 3 out of 20 animals examined. Quantifiable levels of tilmicosin were found in lung tissue with the maximum concentration (1.43±1.13 µg/ml) being recorded on day 10 of medication.

Distribution: Following oral administration, tilmicosin is distributed throughout the body with especially high levels found in the lung and in lung tissue macrophages. It is also distributed in the liver and kidney tissues.

**Rabbits:**
Absorption: When administered orally to rabbits at a dose of 12 mg tilmicosin/kg b.w. as a single dose there is a quick absorption. Maximum concentrations were reached in 30 minutes, being the Cmax obtained of 0.35 µg/ml. Tilmicosin plasma concentrations decreased to 0.1 µg/ml within 2 hours and to 0.02 µg/ml after 8 hours. The elimination half-life was 22 hours.

Distribution: Following oral administration, tilmicosin is distributed throughout the body with especially high levels found in lungs. After 5 days of treatment with medicated feed at a dosage of 200 ppm of product, tilmicosin concentrations in lung tissues were of 192 ± 103 µg/g.

**Applicable to both species:**
Biotransformation: Several metabolites are formed, the predominant one being identified as T1. However the bulk of tilmicosin is excreted unchanged.

Elimination: Following oral administration, tilmicosin is excreted mainly via the bile into the faeces but a small proportion is excreted via the urine.

# 6. PHARMACEUTICAL PARTICULARS

## 6.1 List of excipients

Corn cobs
Liquid paraffin
Macrogolglycerol ricinoleate
Phosphoric acid

## 6.2 Incompatibilities

Do not mix into feed containing bentonite.
In the absence of compatibility studies, this veterinary medicinal product must not be mixed with other veterinary medicinal products.

### 6.3 Shelf life

Shelf-life of the veterinary medicinal product as packaged for sale: 3 years
Shelf life after first opening the immediate packaging: 3 months
Shelf-life after incorporation into meal or pelleted feed: 3 months.

### 6.4 Special precautions for storage

Do not store above 30°C.

Store in the original container.

Store in a dry place.

### 6.5 Nature and composition of immediate packaging

5 and 20 kg polyethylene in paper outer bag

Not all pack sizes may be marketed

### 6.6 Special precautions for the disposal of unused veterinary medicinal product or waste materials derived from the use of such products

Any unused veterinary medicinal product or waste material derived from such veterinary medicinal product should be disposed of in accordance with local requirements.

## 7. MARKETING AUTHORISATION HOLDER

Huvepharma N.V.
Uitbreidingstraat 80
2600 Antwerpen
Belgium

## 8. MARKETING AUTHORISATION NUMBER(S)

## 9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation 11/08/2008

Date of last renewal 12/06/2013

## 10. DATE OF REVISION OF THE TEXT

XX/201X

**PROHIBITION OF SALE, SUPPLY AND/OR USE**

Consideration should be given to official guidance on the incorporation of medicated premixes in final feeds.